

PROCESS FOR THE PREPARATION OF 3, 14 BETA-DIHYDROXY-17-NORMORPHINAN;
CHEMICAL INTERMEDIATE FOR BIOSYNTHESIS OF BUTORPHANOL FROM THEBAIN

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Abstract:

Process for the preparation of 3,14 Beta -dihydroxy-17normorphinan

D R A W I N G

A suitable economic process for the preparation of 3,14 Beta dihydroxy-17-normorphinan of a general formula (I) is being solved, which is a key intermediate of a semisynthetic synthesis of an effective analgesic of Butorphanol from thebaine. Synthesis includes a two step N-demethylation, and concerted dephenoxylation of 4-phenoxy-14 Beta -hydroxy-3-methoxymorphinan in the first step by means of a chloroformate, then, in the second step, by means of sodium action in a liquid ammonia, and by means of the following O-demethylation under action of a complex of aluminium chloride - dialkylsulfide.

Exemplary Claim:

1. Process for the preparation of 3,14 Beta -dihydroxy-17normorphinan having the formula (I)

6-(R-O-), 10a-(HO-)MORPHINAN (I)

wherein R is hydrogen, comprising the reaction of the compound 4-phenoxy-14 Beta -hydroxy-3-R2oxymorphinan having the formula (III)

5-(PHENYL-O-), 6-(R2-O-), 10a-(HO-), 11-(CH3-)MORPHINAN (III)

wherein R2 is hydrogen or methyl, with chloroformate having the formula (V): R3COOCl(V) wherein R3 represents aryl, alkyl or halogenalkyl containing 2 to 4 carbon atoms in alkyl, with an advantage of phenyl, benzyl, ethyl, trichloroethyl or 1-chloroethyl, to produce

the mixture of intermediates having the formula (VI)

5-(PHENYL-O-), 6-(R4-O-), 10a-(R5-O-), 11-R6-MORPHINAN (VI)

wherein R4 is hydrogen, methyl or COOR3, R5 is hydrogen or COOR3, and R6 is COOR3, which will be subjected to a reaction with sodium in a liquid ammonia to produce the compound corresponding to formula (I), wherein on the position R is hydrogen or methyl, without any further isolation and provided that R in formula (I) means methyl, the substance will be subjected to the O-demethylation with a complex of aluminium halide - dialkylsulfide to produce the compound having the formula (I), in which R means hydrogen.

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